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Left ventricular filling in hypertrophic cardiomyopathy
An angiographic study[1]

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In order to study left ventricular filling in hypertrophic cardiomyopathy, left ventricular cineangiograms of 20 patients were digitised frame by frame and compared with those of 10 normal subjects. Peak left ventricular filling rate was 770±260 ml s^{-1} (mean±1 standard deviation), not significantly different from normal. Mitral valve opening was delayed, occurring 140±40 ms after time of minimum cavity area, compared with 93±14 msec in normals ($P<0.01$), indicating abnormal relaxation. Peak left ventricular filling rate was correlated inversely with this delay ($r=0.69$, $P<0.01$), which was greater in patients with angina (155±27 ms) than in those without (85±23 ms) ($P<0.01$). The rapid filling period was also abnormally prolonged in 8 patients. End-diastolic transverse dimension was normal (5·3±0·7 cm) but end-systolic dimension was reduced (2·4±0·4 cm) ($P<0.01$) because of abnormal cavity shape. Peak rate of change of dimension during filling (18·7±5·3 cm s^{-1}) was greater than normal (11·3±3·9 cm s^{-1}) ($P<0.01$), and correlated with peak filling rate ($r=0.82$, $P<0.001$). Thus, peak filling rate is normal in hypertrophic cardiomyopathy, but the filling pattern may be abnormal, apparently because of impaired relaxation and abnormal cavity shape rather than mechanical obstruction to inflow.

A significant component of the overall impairment of cardiac function in hypertrophic cardiomyopathy appears to be the abnormal diastolic function of the left ventricle (Hansen *et al.*, 1962; Goodwin, 1974). It has been suggested that increased elastic stiffness of the myocardium may be associated with a reduced rate of filling (Oakley, 1971) and indirect evidence for this has been obtained from the left atrial pressure pulse (Stewart *et al.*, 1968) and from the mitral echogram (Moreyra *et al.*, 1969). On the other hand, ventriculographic studies in a small number of patients have shown filling rates are within the normal range (Holt *et al.*, 1969; Hammermeister and Warbasse, 1974).

It was the purpose of the present study to examine the left ventricular filling pattern in a larger series of patients with hypertrophic cardiomyopathy. Since the limitations of ventriculographic volume analysis are greater when the left ventricle is small and irregular in shape, we have also used other methods of investigating the filling pattern during diastole. An attempt was made to elucidate the mechanisms by which these volume changes were brought about, and the findings were correlated with the clinical features of the condition.

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Patients and methods

Twenty patients, 13 of whom were men, were studied after a diagnosis of hypertrophic cardiomyopathy had been made on ventriculographic criteria (Braunwald *et al.*, 1964). Clinical details are given in Table 1. The case records were examined retrospectively, with particular reference to the occurrence of angina or dyspnoea on exertion, heart size on chest radiography, the degree of left ventricular hypertrophy on electrocardiogram, left ventricular end-diastolic pressure, the degree of outflow tract obstruction, and the presence or absence of significant mitral regurgitation. Only 1 patient had been taking propranolol, which was stopped 5 days before diastolic ventriculography.

A second group of 10 patients was also studied. These complained of chest pain, but no haemodynamic or angiocardiographic abnormality of the heart or coronary arteries was found. This group is referred to as 'normal' though it is recognised that

Table 1 *Details of patients*

Case No.	Age (y)	Sex	Symptoms	NYHA grading	Heart* rate	Heart size (transverse diameter) on chest radiograph (cm)	Degree of LVH on ECG	End diastolic pressure (mmHg)	Mitral regurgitation	Presence or absence of LV outflow tract gradient At rest	After provocation†
1	29	F	Dyspnoea; palpitation with chest pain	II	85	12·5	±	25	Nil	+	+
2	39	M	Syncope	III	85	15·5	+	15	Slight	0	+
3	46	M	Dyspnoea	I	65	18·0	+	30	Slight	0	+
4	57	M	Dyspnoea; angina	III	90	14·0	±	10	Slight	+	+
5	41	M	Dyspnoea; angina	II	80	13·5	+++	20	Nil	0	0
6	57	F	Dyspnoea; angina	II	73	14·0	+++	—	Nil	0	++
7	27	M	Episodic dyspnoea, dizziness, and chest pain	III	100	13·5	+	16	Nil	0	+
8	56	F	Dyspnoea	II	75	13·5	LBBB	30	Gross	+	+
9	31	M	Palpitation	I	85	16·0	++	—	Nil	0	++
10	54	F	Dyspnoea; angina	II	67	14·0	0	15	Moderate	0	+
11	12	M	Dyspnoea; angina	II	90	14·0	++	12	Moderate	+	+
12	53	M	Dysnpoea; angina	II	75	14·5	++	18	Nil	0	+
13	26	M	Dyspnoea; angina	II	92	16·5	+++	20	Nil	0	0
14	52	F	Dyspnoea; angina	II	75	15·5	++	28	Nil	0	+++
15	50	M	Dyspnoea; angina	III	87	15·0	+	17	Slight	0	0
16	62	F	Dyspnoea; angina	III	67	13·0	±	16	Nil	+	0
17	44	M	Dyspnoea; angina	III	63	14·0	+++	30	Nil	0	+
18	33	M	Dyspnoea; angina	III	73	18·0	+++	—	Slight	+	+
19	51	F	Dyspnoea; angina	III	75	12·5	0	—	Slight	0	+
20	40	M	Palpitation; angina	II	60	14·0	+++	22	Moderate	0	++

*Derived from cycle length.
†Provocation by amyl nitrite inhalation or by ventricular ectopics.

minor or hitherto undescribed abnormalities may have been present.

CARDIAC CATHETERISATION AND ANGIOCARDIOGRAPHY

The patients were studied fasting, and were premedicated with diazepam. Right and left heart catheterisation was performed, either using the Seldinger method from the right femoral artery and vein or a cut-down right antecubital fossa. Pressures were measured with a fluid-filled manometer system and referred to the mid-thorax. An injection of 35 to 50 ml Triosil was made into the left ventricle at 10 ml per second, and cine film exposed at 48 frames per second. Calibration was performed by means of a grid at mid-chest level. Ectopic and postectopic beats were not studied.

DIGITISATION

Left ventricular cineangiocardiograms were digitised using methods that have previously been described (Gibson and Brown, 1975a). Successive frames of the beat to be studied were projected on to the digitising table, starting at end-diastole, and the perimeter of the cavity was traced using a cursor, starting from the aortic root.

ANALYSIS OF DATA

Plots were made of cavity area, derived by numerical integration, cavity perimeter, and long axis, representing the distance from the mid-point of the aortic root to the furthest point on the cavity perimeter (Fig. 1). Estimates of cavity volume and its rate of change were made using an area–length formula, based on an ellipsoidal model for the left ventricle (Dodge *et al.*, 1966). Shape index[1] (Gibson and Brown, 1975b) was also plotted; this function, which is independent of cavity size, has a maximum value of 1 when the cavity outline is circular, and a minimum of zero when cavity obliteration occurs. Plots were also made of a transverse left ventricular dimension and its rate of change, approximately at the level of the mitral valve (Gibson and Brown, 1975a) (Fig. 2). From these curves the following information was derived for each patient:

(1) Left ventricular volumes

End-systolic and end-diastolic volumes were calculated and then the ejection fraction was derived in the usual way. The peak rate of increase of left ventricular volume during the rapid phase of ventricular filling was also measured, and the increase in volume during left atrial systole was expressed as a percentage of the total volume change during diastole.

(2) Left ventricular dimension

End-systolic and end-diastolic transverse left ventricular dimensions, above the level of the

[1]Shape index $= 4\pi$ area/perimeter^2.

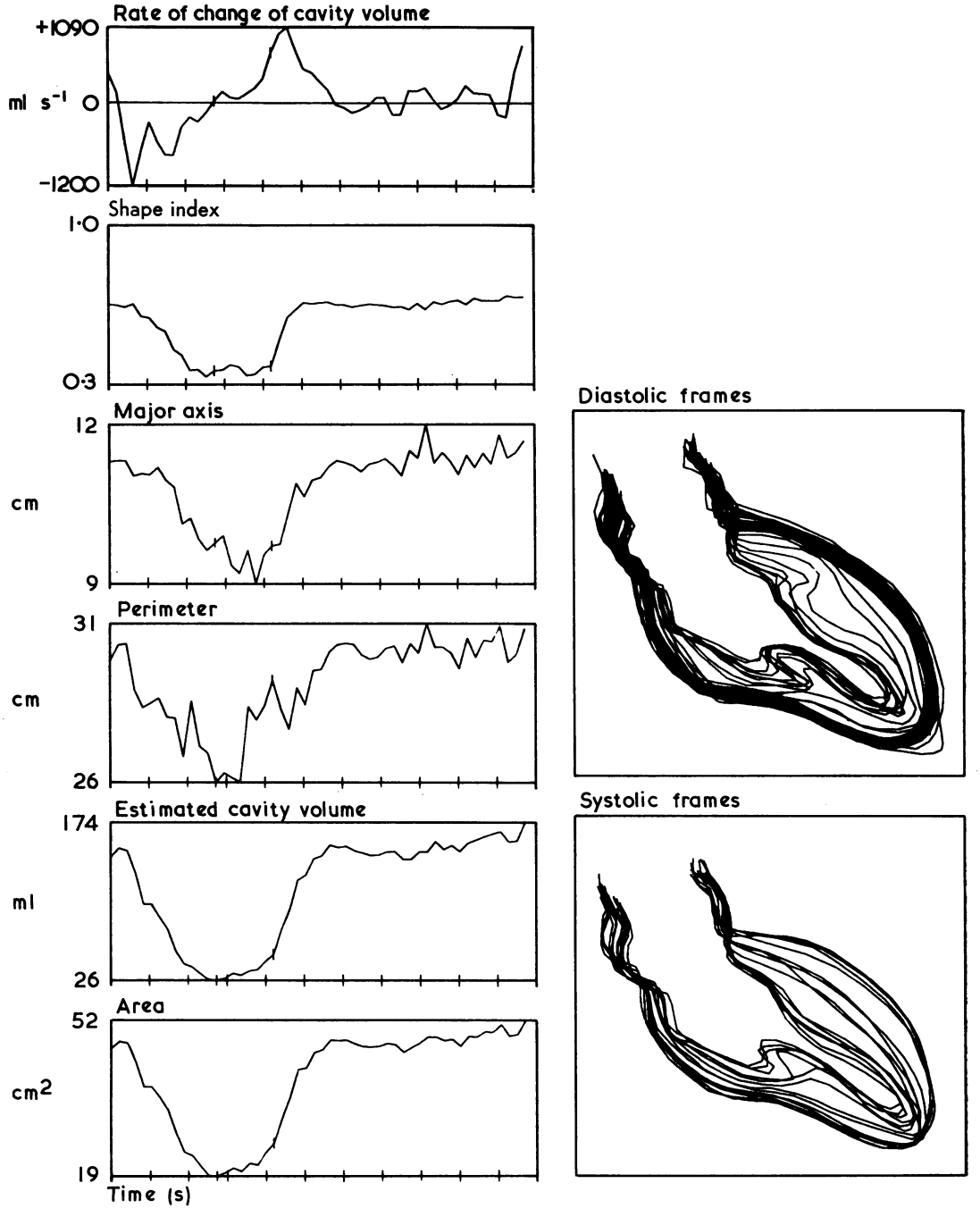

Fig. 1 *Plots of cavity area, long axis, perimeter, shape index, estimated cavity volume, and rate of change of volume. Vertical lines indicate minimum cavity area and mitral valve opening. Superimposed cavity outlines during systole (lower) and diastole (upper) are shown on the right (case 20, second beat).*

papillary muscles, and peak rate of change of dimension during early diastole were measured.

(3) Cavity configuration

End-systolic and end-diastolic shape indices were calculated, together with the change in shape index between the time of minimum cavity area and mitral valve opening.

(4) Diastolic time intervals

The time of minimum cavity area at end-ejection was identified. After this there is a slight increase in cavity area until the time of mitral valve opening (Ruttley *et al.*, 1974), taken as the frame in which unopacified blood from the left atrium first appears within the left ventricular cavity. The end of rapid filling could nearly always be identified as a clearly defined discontinuity on the curves of cavity volume and its rate of change with time (Straub, 1910). In the few patients in whom filling continued at an approximately constant rate until the end of the cardiac cycle with no recognisable period of diastasis, end-diastole was taken as the end of rapid filling.

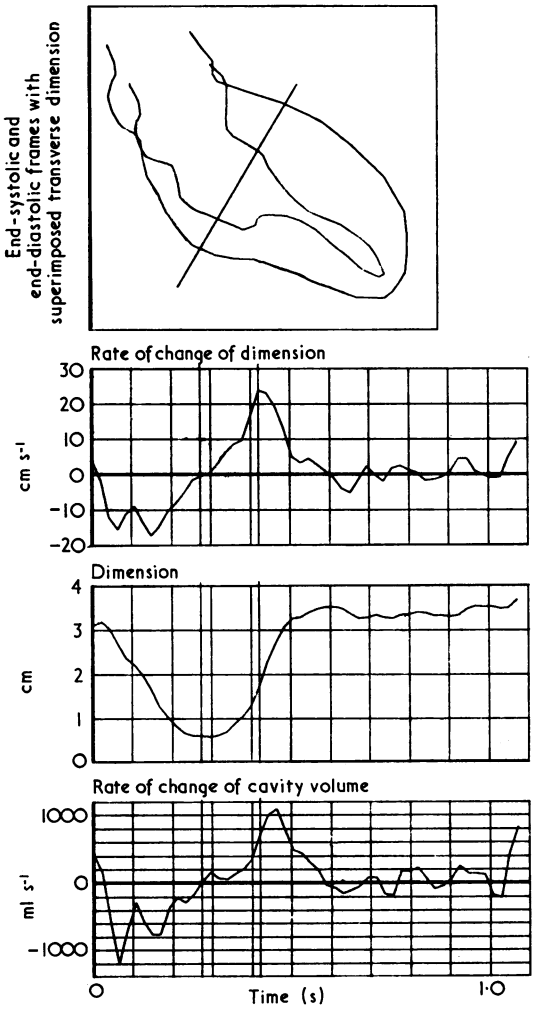

Fig. 2 *The uppermost plot shows the position of the chosen transverse dimension superimposed on the digitised outlines of the end-systolic and end-diastolic frames. Other plots show dimension, rate of change of dimension, and rate of change of estimated cavity volume (same patient as Fig. 1).*

Diastole could thus be subdivided into:

(i) The isovolumic relaxation time, from the time of minimum cavity area to mitral valve opening,

(ii) a period of rapid filling from mitral valve opening until the discontinuity on the volume curve, and

(iii) the period of diastasis and atrial systole.

The mean rate of rapid filling was calculated as the volume change between mitral valve opening and the discontinuity divided by the time interval between these two events.

OVERALL PATTERN OF WALL MOVEMENT

A general picture of left ventricular wall movement was obtained by superimposing cavity outlines, those from the start of the beat to the outline with the smallest area being taken as systolic, and the remainder as diastolic (Fig. 1). A more comprehensive display of wall movement was also used which was developed for the study of regional abnormalities occurring in ischaemic heart disease (Gibson *et al.*, 1976) (Fig. 3). Forty equally spaced points were identified on the end-diastolic cavity outline, starting from the mitral aspect of the aortic root and proceeding anti-clockwise. From each of these points, the nearest point on the end-systolic frame was sought. Wall movement was then plotted against time along each of the 40 lines thus defined. These plots were then stacked obliquely as an isometric display, with upward displacement on each representing inward movement. A series of lines joining simultaneous events were superimposed, those representing minimum cavity and mitral valve opening being accentuated. This display illustrates regional abnormalities of wall movement to, and their timing in, the cardiac cycle. From this display, the region of maximum outward wall movement during the period of isovolumic relaxation was identified, and its amplitude measured in the anterior and inferior regions of the ventricle.

Reproducibility

The reproducibility of the digitising technique for the analysis of cineangiograms has previously been

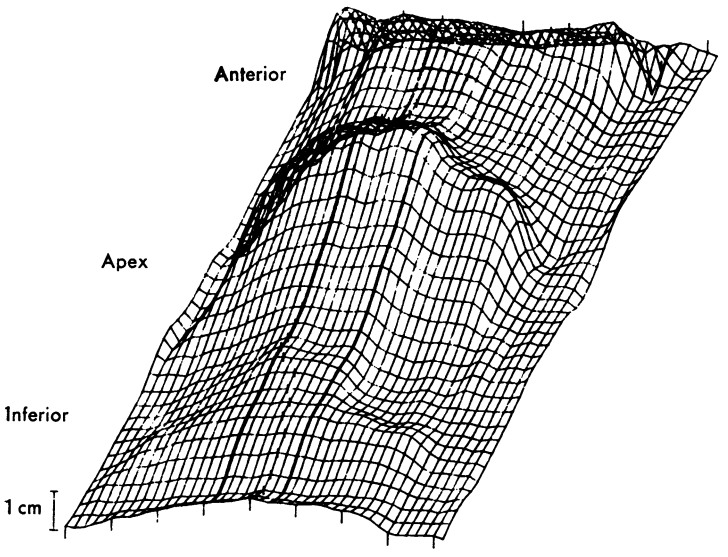

Fig. 3 *Plot of regional wall movement against time after the start of systole from the left ventriculogram (case 20). Each horizontal plot represents wall movement at one site around the perimeter of the cavity. Upward displacement represents inward movement. The diagonal lines are isochrones connecting events occurring simultaneously. The two accentuated isochrones show the times of minimum cavity area and mitral valve opening. 1 cm calibration is shown (bottom left).*

described (Gibson and Brown, 1975b). In view of the abnormal cavity shape, a separate assessment was made in the present study in 8 patients. Two consecutive beats and also two separate determinations of the same beat were analysed. The results are shown in Table 2, expressed as mean percentage error between pairs of observations.

Statistical methods

Student's t tests were used to assess the statistical significance of differences between means. Normal ranges are defined as a range of ± 2 standard deviations about the corresponding mean of the normal group. Regression analysis was performed by the method of least squares.

Results

LEFT VENTRICULAR VOLUMES (Table 3)

Left ventricular end-diastolic and end-systolic volumes were within the normal range in all patients. There was considerable variation in peak rate of increase of volume during rapid filling, with a mean value for the group of 770 ± 260 ml s^{-1}, compared with the normal value of 610 ± 210 ml s^{-1}. When individual values were considered, the peak rate of increase of volume was greater than normal in 4 patients, all the remainder being within the normal range. Mean filling rate during early diastole was within the normal range in all except one patient with severe mitral regurgitation, in whom it was increased (1040 ml s^{-1}). In 8 patients in whom a separate atrial contribution was detectable, this amounted to 17 per cent (1 to 23%) of the total diastolic blood flow into the left ventricle.

LEFT VENTRICULAR DIMENSION (Table 4)

The mean end-diastolic dimension in the patients with hypertrophic cardiomyopathy was $5{\cdot}3 \pm 0{\cdot}7$ cm, not significantly different from normal, though values from the two patients with the largest end-diastolic volumes were outside the normal range. Mean end-systolic dimension was $2{\cdot}4 \pm 0{\cdot}4$ cm, significantly less than normal ($P < 0{\cdot}01$). The peak rate of increase of dimension was $18{\cdot}5 \pm 5{\cdot}3$ cm s^{-1}, compared with the normal value of $11{\cdot}0 \pm 3{\cdot}9$ cm s^{-1}. In the patients with hypertrophic cardiomyopathy, there was significant correlation with peak rate of increase of volume, with the linear regression equation: peak rate of increase of volume $= 41$ (peak rate of increase of dimension) $+ 8{\cdot}5$: $r = 0{\cdot}82$; standard error of the estimate $= 156$.

DIASTOLIC TIME INTERVALS

The mean isovolumic relaxation period in patients with hypertrophic cardiomyopathy was 140 ± 40 ms, significantly greater than normal (93 ± 14 ms) ($P < 0{\cdot}01$). There was a negative correlation

Table 2 *Reproducibility studies (8 patients)*

	Mean percentage difference between repeat determinations	
	Same beat	*Consecutive beats*
Peak rate of increase of volume	10·3%	15·5%
End-diastolic volume	11·4%	12·5%
Isovolumic relaxation period	9·0%	5·0%
Rapid filling period	9·5%	9·0%

Table 3 *Analysis of cineangiograms*

Case No.	Peak diastolic filling rate (ml s^{-1})	Mean diastolic filling rate (ml s^{-1})	EDV (cm^3)	EF (%)	IRP (ms)	Time to peak filling (ms)	RFP (ms)	Shape index	
								End-systole	End-diastole
1	926	740	143	88	130	150	140	0·45	0·66
2	978	705	193	80	50	115	170	0·57	0·75
3	1213	700	174	80	90	105	130	0·45	0·64
4	1141	600	109	83	130	150	120	0·55	0·75
5	476	245	77	83	190	230	130	0·60	0·60
6	520	375	134	87	165	170	295	0·50	0·70
7	574	510	109	87	150	170	110	0·35	0·55
8	1302	1040	190	90	100	120	120	0·40	0·65
9	1008	800	132	81	100	130	110	0·35	0·55
10	699	480	136	88	140	180	190	0·40	0·70
11	640	615	164	88	120	150	210	0·35	0·55
12	750	520	146	83	170	240	180	0·45	0·65
13	873	630	131	82	130	170	130	0·40	0·55
14	659	415	150	81	210	350	250	0·40	0·60
15	579	325	68	83	160	230	125	0·40	0·58
16	543	365	82	92	125	200	130	0·42	0·65
17	383	230	93	83	200	—	210	0·45	0·55
18	620	455	199	88	150	200	250	0·40	0·60
19	584	400	115	82	150	170	165	0·55	0·63
20	978	700	156	80	145	170	125	0·40	0·65
HCM*	770 ±260	540 ±200	140 ±40	84 ±4	140 ±40	180 ±60	160 ±50	0·44 ±0·07	0·63 ±0·06
Normals*	610 ±210	460 ±170	120 ±40	80 ±6	93 ±14	150 ±40	130 ±20	0·65 ±0·03	0·84 ±0·04

EDV, end-diastolic volume; IRP, isovolumic relaxation period; HCM, hypertrophic cardiomyopathy; EF, ejection fraction; RFP, rapid filling period.
* = Mean values ± SD.

Table 4 *Analysis of transverse diameter*

	End-systolic* (cm)	End-diastolic* (cm)	Peak diastolic rate of change* (cm s^{-1})	Rapid filling period* (ms)
Hypertrophic cardiomyopathy	2·4 ±0·4	5·3 ±0·7	18·7 ±5·3	160 ±64
Normal	3·7 ±0·4	5·1 ±0·5	11·0 ±3·9	130 ±20

*Mean ± SD.

between isovolumic relaxation period and peak rate of increase of volume ($r = -0·69$, $P < 0·01$) (Fig. 4), and between isovolumic relaxation period and mean rate of increase of volume during the rapid filling period ($r = -0·70$, $P < 0·01$). The mean time from mitral valve opening to the end of the rapid filling period was 160 ±50 ms, estimated from the left ventricular volume record, compared with a normal value of 130 ±20 ms. The duration of the rapid filling period was also estimated from the transverse left ventricular dimension record as the interval between mitral valve opening and the discontinuity; this also gave a mean value of 160 ±65 ms.

CAVITY CONFIGURATION

The end-diastolic shape index had a mean value of 0·63 ±0·06, which was significantly less than normal, 0·85 ±0·04 ($P < 0·001$). The end-systolic value was 0·44 ±0·07 compared with a value of 0·65 ±0·03 in the normal group ($P < 0·001$). Representative displays of wall movement are given in Fig. 1 and 3. Mean outward wall movement during the isovolumic relaxation period was 4·7 ±2·8 mm along the anterior border and 3·6 ± 2·4 mm along the inferior. These values are not significantly different from normal. In no patient was inward wall movement observed during the isovolumic period, nor were localised abnormalities observed as in ischaemic heart disease (Gibson *et al.*, 1976). The mean shape index change during isovolumic relaxation (0·05 ±0·06) was also not significantly different from normal (0·06 ±0·02).

CLINICAL FEATURES

No relation was apparent between the pattern of left ventricular filling and the degree of dyspnoea, heart size on chest radiograph, the degree of left ventricular hypertrophy on electrocardiogram, end-diastolic pressure in the left ventricle, or the degree of outflow tract obstruction. Though the patient with the most rapid filling rate had mitral regurgitation, this was not a consistent relation in the group as a whole. There did, however, appear to be a strong association between the presence or absence of angina and the degree of diastolic

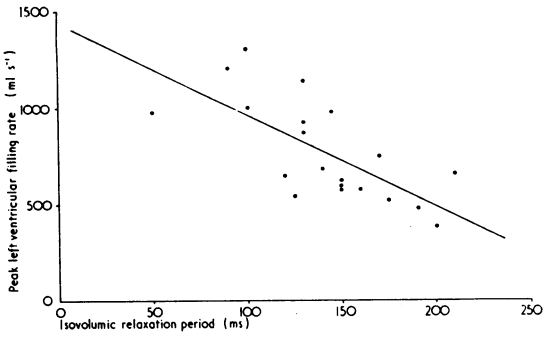

Fig. 4 *Relation between the isovolumic relaxation period and the peak diastolic filling rate. Simple linear regression line shown.*

abnormality. In patients with angina, isovolumic relaxation times were significantly longer than in those without, and peak filling rates were lower (Fig. 5 and 6).

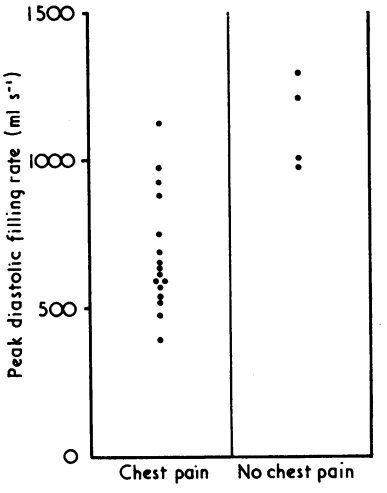

Fig. 6 *Relation between peak filling rate and presence of chest pain.*

Discussion

Measurement of left ventricular volume by angiography is subject to particular technical limitations in hypertrophic cardiomyopathy. The irregular shape of the cavity as outlined by radio-opaque dye is quite unlike any simple geometrical figure, and the trabeculations give it a ragged edge that cannot be completely digitised using the present method. A major problem in hypertrophic cardiomyopathy is presented by the hypertrophied papillary muscles. Though these occupy a significant part of the small cavity volume, with a corresponding reduction in the volume of blood contained in it, this is not reflected in angiographic estimates. More important, at end-diastole, the papillary muscles are within the cavity as defined by angiography, while at end-systole, they form its outer border. Thus, during early diastolic filling, there is a time when dye-containing blood first penetrates the space outside the papillary muscles, with a corresponding increase in projected area. Though this represents a true increase in cavity size, it is not associated with a corresponding amount of blood flow across the mitral valve. It is clear, therefore, that in patients with hypertrophic cardiomyopathy estimates of peak filling rates derived from left ventricular volume changes measured by angiography may be in error and, in particular, it is possible that peak rates of changes may represent movement of the papillary muscles rather than flow through the mitral valve. We have attempted to avoid these difficulties in two ways. The duration of the rapid filling phase can readily be measured in normal subjects and in the majority of patients with hypertrophic cardiomyopathy as the time interval between mitral valve opening and a discontinuity on the volume curve representing the onset of diastasis. This time interval was used to calculate the mean rate of increase of volume during rapid filling, which was shown both in normal subjects and in patients with hypertrophic cardiomyopathy to correlate closely with peak values. Secondly, it was possible to study the transverse dimension of the cavity at the level of the mitral valve, in a region of

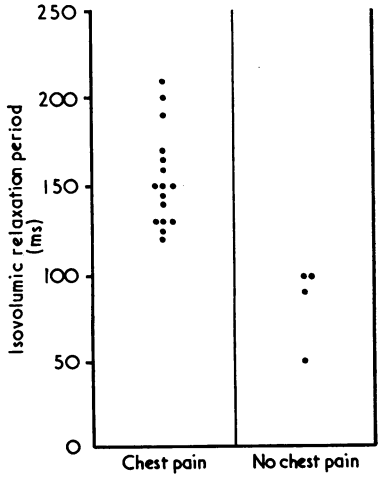

Fig. 5 *Relation between isovolumic relaxation period and presence of chest pain.*

the ventricle above the papillary muscles, where trabeculation is less conspicuous. Peak rates of change of volume correlated closely with those of dimension, and estimates of the time of onset of diastasis made by the two methods were also very similar. It seems, therefore, that in spite of the very abnormal left ventricular cavity shape, measurement of either transverse dimension or volume can be used to assess filling pattern in hypertrophic cardiomyopathy. The same problems affect measurement of shape index which also depends on definition of the cavity perimeter. However, the effect of any smoothing introduced during the digitising process is to reduce the perimeter, thus overestimating shape index, particularly at end-systole, so that any error in the present study is towards underestimating the magnitude of changes in cavity shape during the cardiac cycle.

It is well documented that the properties of the left ventricular wall are abnormal in hypertrophic cardiomyopathy. End-diastolic pressure may be greatly increased in spite of a normal or even reduced end-diastolic volume. Increased passive elastic stiffness or reduced compliance have been reported, as might be anticipated on the basis of the very abnormal structure of the myocardium. It may seem surprising, therefore, that in spite of these abnormalities, early diastolic filling is able to proceed at a normal rate as was found in this study. In order to reconcile our results with these observations, it must be stressed that any description of the properties of the ventricle using terms such as compliance or elastic stiffness, presupposes that it is behaving in a static and passive manner (Mirsky, 1976) which is a very specific type of mechanical behaviour. There is no evidence to suggest that the ventricular wall does behave in this way during early diastole, and indeed there is much to the contrary. Ventricular volume increases while pressure is still dropping, a situation that is clearly not passive, as the properties of the ventricle are changing rapidly with time (Katz, 1930; Dodge *et al.*, 1962; Porter *et al.*, 1971). Similarly, in mid-diastole, transverse diameter can increase with little or no change in estimated wall stress (Gibson and Brown, 1974), suggesting that filling at this stage is mediated by reorientation rather than stretching of muscle fibres. One way in which this could occur is by a change in cavity shape towards a more spherical configuration. Only during late diastole does the ventricle show simple elastic behaviour, and only at this time, therefore, would the effects of abnormal wall stiffness become apparent. The results of the present study are compatible with these ideas. Left ventricular shape index in hypertrophic cardiomyopathy was significantly lower at end-diastole than in the normal group, and the change with systole was proportionately greater indicating that more of the inflow was accommodated by a change in cavity shape. The results thus support the idea of an altered mechanism of left ventricular filling in hypertrophic cardiomyopathy in which volume changes are mediated to a greater extent by changes in cavity shape, representing an adaptation to the increased stiffness of the myocardium. During atrial systole, when this mechanism does not operate, reduced ventricular compliance causes the increase in left ventricular volume to be within normal limits in spite of the large increase in end-diastolic pressure that may occur in these patients (Bruns, 1970; Hammermeister and Warbasse, 1974).

Other diastolic abnormalities in patients with hypertrophic cardiomyopathy have been defined in this study. The isovolumic relaxation time, defined as the interval between minimum cavity area and mitral valve opening, was found to be significantly prolonged. This probably reflects a reduced rate of fall of left ventricular pressure, since aortic or left atrial pressure would have had to be well outside the physiological range to have caused this abnormality. This prolongation of ventricular relaxation appears to be a primary abnormality in hypertrophic cardiomyopathy. It is likely to have caused the increase in time interval between aortic valve closure and the 'O' point of the apex cardiogram previously reported in a similar group of patients (Hubner *et al.*, 1973; Goodwin, 1974; Hardarson, 1974). However, the 'O' point may occur up to 150 ms after mitral valve opening, so that this interval also includes a significant part of the early rapid phase of ventricular filling (Prewitt *et al.*, 1975).

It has been suggested that left ventricular inflow tract obstruction may occur in hypertrophic cardiomyopathy, similar to that caused by mitral stenosis (Shabetai and Davidson, 1972; Feizi and Emanuel, 1975). Left ventricular filling in mitral stenosis differs from normal, not only in that the peak rate of increase of volume is reduced, but also in that the pattern of an early diastolic rapid filling phase followed by diastasis is lost and replaced by a lower rate of filling maintained for a longer period. In the present patients, peak rates of increase of volume were normal, but in 8 the duration of the rapid filling phase was prolonged beyond the upper limit of normal of 170 ms, so that the filling pattern did to some extent resemble that in mitral stenosis. Though it is possible that this prolonged rapid filling phase resulted from mechanical obstruction to inflow, its relation in individual patients to the delay in mitral valve opening (Fig.

4) suggests that it is already determined before filling starts, and is thus more likely to be a further manifestation of abnormal relaxation. The disturbances of function described here may be a reflection of the abnormal structure of the left ventricle in hypertrophic cardiomyopathy. Not only is the wall of the ventricle very considerably thickened, but also the usual arrangement of muscle fibres is disturbed to a variable extent by the presence of foci in which myocardial architecture is distorted by irregularly arranged bizarre muscle cells (Olsen, 1971; Van Noorden *et al.*, 1971; Ferrans *et al.*, 1972). It is thus possible that prolonged relaxation may occur in patients in whom these abnormal areas are more extensive, while increased wall stiffness may be a function of hypertrophy of normal myocardial cells, linearly arranged.

These early diastolic abnormalities in hypertrophic cardiomyopathy may be compared with those in ischaemic heart disease. Delayed mitral valve opening has also been observed in patients with ischaemic heart disease when it is frequently associated with complex changes in cavity shape during isovolumic relaxation related to the pattern of coronary arterial involvement (Gibson *et al.*, 1976). In contrast, delayed mitral valve opening in hypertrophic cardiomyopathy was found to be associated with uniform wall movement and was not accompanied by any significant change in cavity shape. The correlation between a prolonged relaxation period and a history of anginal pain was a suggestive one in our patients, and appeared sufficiently clear-cut to be significant in individuals. The greater part of coronary blood flow takes place in diastole (Gregg and Fisher, 1963), and only at this time in the subendocardial layers (Kirk and Honig, 1964). Prolonged isovolumic relaxation might be expected to reduce subendocardial blood flow, particularly when the duration of diastole is further reduced by tachycardia. The resemblance between events during isovolumic relaxation in patients with ischaemic heart disease and in those with hypertrophic cardiomyopathy raises the possibility that angina in the two conditions may have a similar basis.

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